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EXAMINER

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.



## **DETAILED ACTION**

The amendment filed January 31, 2008 have been received and entered into the application.

### **Action Summary**

The rejection of claims 25-35 and 37 under 35 U.S.C. 103(a) as being unpatentable over Nagabhushan (U.S.Patent No. 4,311,857) in view of Bundgaard (1985) is being maintained for the reasons stated in the previous Office Action. However, the rejection is modified in this Office Action to include newly added claim 49 and to exclude allowable claims 34, 35 and 37.

The rejection of claim 36 under 35 U.S.C. 103(a) as being unpatentable over Nagabhushan (U.S.Patent No. 4,311,857) in view of Bundgaard (1985) as applied to claims 25-35 above, and further in view of Shuster et al. (US 2004/0198704 A1) is hereby expressly withdrawn in view of Applicants' declaration.

### ***Allowable Subject Matter***

In view of Applicants' declaration, claims 34-37 are allowed.

### ***Response to Arguments***

Applicants' arguments filed January 31, 2008 have been fully considered but they are not persuasive. Applicants essentially argue that the composition claimed in claim 25, which includes the combination of a first ester prodrug of florfenicol and a second ester prodrug of florfenicol formulated as a composition for administration to a mammal by injection, however, has unexpected advantages that are not disclosed or suggested in either Nagabhushan or Bundgaard. This is not found persuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one of ordinary skill in the art to employ ester derivatives of florfenicol including florfenicol propionate and florfenicol acetate etc.. taught by Nagabhushan in a single formulation for parenteral administration because ester prodrugs taught by Nagabhushan have beneficial effect in parenteral formulation because of they increase the aqueous solubility of drugs containing a hydroxyl group such as florfenicol and this is well known and recognized effective means of preparing parenteral formulation as taught by Bundgaard. The cited references teach the common utility of florfenicol in ester formulation. The motivation for combining the components flows from their individually known common utility (see *In re Kerkhoven*, 205 USPQ 1069 (CCPPA

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1980)). Therefore, the claimed invention, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25-33 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagabhushan (U.S. Patent No. 4,311,857) of record in view of Bundgaard (1985).

Nagabhushan teaches a pharmaceutical composition comprising D-(threo)-1-p-methylsulfonylphenyl-2-chloroacetamido-3-fluoro-1-propanol (also known as **florfenicol**) together with a compatible pharmaceutically acceptable carrier. (column 10, lines 5-10, column 20 lines 10-11). Nagabhushan demonstrates that above composition can be formulated in an injectable solution with concentration of 250mg/ml of florfenicol as an active drug. (column 11, lines 20-31, column 12, lines 55-61, Formulation 5). Nagabhushan teaches that the ester derivatives of florfenicol including formic, acetic, propionic, triethylacetic, **butyric**, isobutyric and valeric etc., are also antibacterially active as florfenicol. (column 4 lines 22-60). Nagabhushan teaches that the composition can be formulated to be administered parenterally via intramuscular injection and that the dosage to be administered depends on the stage and severity of

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the injection, the susceptibility of the infecting organism to the antibacterial and the individual characteristics of the animal species being treated. (column 10, lines 55-66). Nagabhushan teaches that **propylene glycol** is compatible with florfenicol. (column 11, lines 5-20, formulations).

Nagabhushan does not expressly teaches combinations of florfenicol esters in a single formulation and the specific concentration of florfenicol.

Bundgaard teaches that ester formation has long been recognized as an effective means of increasing the aqueous solubility of drugs containing a hydroxyl group, with the aim of developing prodrug preparation suitable for parenteral administration. (page 7, last sentence). Bundgaard teaches that esters convert rapidly in vivo to the active parent drug by hydrolysis. (page 8, second paragraph).

It would have been obvious to one of ordinary skill in the art to employ ester derivatives of florfenicol including florfenicol butyrate, florfenicol propionate and florfenicol acetate etc.. taught by Nagabhushan in a single formulation for parenteral administration because ester prodrugs taught by Nagabhushan have beneficial effect in parenteral formulation because of they increase the aqueous solubility of drugs containing a hydroxyl group such as florfenicol and this is well known and recognized effective means of preparing parenteral formulation as taught by Bundgaard. One would have been motivated to make such a modification in order to achieve the active florfenicol in vivo rapidly by hydrolysis of prodrug of florfenicol ester taught by Nagabhushan. Further, to employ more than one active esters of florfenicol in a single formulation is obvious because each of the esters of florfenicol have antibacterial

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activity as taught by Nagabhushan. The motivation for combining the components flows from their individually known common utility (see *In re Kerkhoven*, 205 USPQ 1069(CCPA 1980)). With regard to the property of the composition forms a drug depot when injected into a mammal is obvious because the obvious composition taught by Nagabhushan as modified by Bundgaard constitutes with the same active agents cannot have mutually exclusive properties. Further, the specific concentration of florfenicol set forth in the claim is obvious because Nagabhushan demonstrates injectable composition of active agent in concentration of 250mg/ml and that the dosage to be administered depends on the stage and severity of the infection, the susceptibility of the infecting organism to the antibacterial and the individual characteristics of the animal species being treated. Therefore, one of ordinary skill in the art would have been motivated to optimize the concentrations of the parenteral formulation of Nagabhushan as modified by Bundgaard for the specific individuals being treated as determined by their diagnosis and the progress in their condition.

**THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

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Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/  
Primary Examiner, Art Unit 1617

Jmk  
April 25, 2008